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EXAMINER

BERTOGLIO, VALARIE E

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 02/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/892,206	BRENNAN ET AL.
	Examiner	Art Unit
	Valarie Bertoglio	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 12/19/2002.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-33 is/are pending in the application.

4a) Of the above claim(s) 1-4, 13-16, and 31-33 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 5-12 and 17-30 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). _____.

2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 and 8. 6) Other: _____.

Election/Restrictions

Applicant's election with traverse of Invention III, claims 8 and 17-25 in paper No. 14, dated 12/23/2002 is acknowledged. It has been determined that it would not require undue burden on the part of the examiner to examine Groups II-V together. While the restriction on the basis that the claimed inventions are patentably distinct is still held proper, Groups II-V have been rejoined in this action.

The traversal is partially on the ground(s) that a search of Invention I claims and Invention II-VI or Invention VII claims together would not be an undue burden because a reasonable search would produce results related to the targeting construct of Invention I and the cells of Invention II or the animals of Invention III or the methods of screening using the transgenic animal of Invention IV, or the methods of making a transgenic animal of Invention V, or the methods of screening using the transgenic cells of Invention VI, or the agents of Invention VII. This argument is not found persuasive because it is maintained that each of the inventions of Invention I and Invention II-VI or VII require a separate search status on the basis of each of Inventions II-VII requiring a materially different product from that of Invention I, which is separately classified. In particular, Invention I is directed to methods of making a gene targeting construct that is not necessary to disrupt the anaphylatoxin C3a receptor in cells or in animals. Materially different constructs can be used to disrupt anaphylatoxin C3a receptor. Furthermore, the nucleic acid sequences of Invention I and the cells of Invention II or the animals of Invention III are structurally and functionally different and have different uses. As such, Invention I and Invention II or Invention III require materially different reagents and technical considerations such that a proper search for both inventions would require an extensive search for materially different methods thereby placing an undue search burden upon the Examiner. Furthermore, the nucleic acid of Invention I and the agents of Invention VII are structurally and functionally

distinct. The nucleic acid is not required for the compounds and the compounds are not necessary for the nucleic acid. The nucleic acid is not necessary for the methods of Inventions IV, V or VI. The cells, the animal and the modulators and the methods of using said products have distinct and different purposes from the nucleic acid construct. Therefore, it is maintained that the Invention I and Invention II-VI or VII are distinct due to distinct structures, classification and method steps and are thus, separately classified and searched.

The traversal is partially on the ground(s) that a search Invention II-V or VI and the agent of Invention VII together would not be an undue burden. The examiner maintains that Invention II-V or VI and Invention VII are patentably distinct because the cells of Invention II, the transgenic animal of Invention III, the methods of using a transgenic animal of Invention IV, the methods of making a transgenic animal of Invention V, the methods of using cells to screen for modulators of Invention VI do not require the agent of Invention VII and the agent does not require any of Inventions II-VI. The cells, the animal and the modulators have distinct and different purposes from the agent. Furthermore, the burden required to search the Inventions II-V or VI with the agent of Invention VII, which has a different classification, would be undue.

The traversal is partially on the ground(s) that a search of the cells of Invention II or the transgenic animals of Invention III and the methods of identifying agents of Invention VI or the agent of Invention VII together would not be an undue burden. The examiner maintains that Inventions II or III and Invention VI or VII are patentably distinct because the cells or animals are structurally and functionally distinct from the compounds. The cells or animals can be used for in vitro assays, to study function of anaphylatoxin C3a receptor, to produce proteins, or to test gene expression while the compounds can be used to modulate gene expression. The cells or animals each have a distinct and different purpose from the compounds. The methods of Invention VI do not utilize the animals of Invention III. The examiner maintains that Inventions II

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or III and Inventions VI or VII are structurally and functionally distinct, have different purpose and use, and are classified differently. Furthermore, the burden required to search the cells or animals with the compounds, which have a different classification, would be undue.

The traversal is partially on the ground(s) that a search of the methods Invention IV encompassing use of a transgenic animal together with the methods of Invention VI encompassing methods of using cells to screen agent would not place undue burden on the examiner as they are related in purpose. The examiner maintains that the methods of Inventions IV and VI are materially different and plurally independent from each other and are practiced with materially different process steps and technical considerations.

The traversal is partially on the ground(s) that a search of the methods of making (Invention V) and using a transgenic animal (Invention IV) or methods of using cells (Invention VI) and the agent of Invention VII together would not be an undue burden. The examiner maintains that the methods of making and using a transgenic animal or cells and the agents are patentably distinct because the animals and cells are structurally and functionally distinct from the compounds. Neither the animals nor the cells are necessary for the compounds, nor are the compounds necessary for the methods of using the animals or cells. Furthermore, the burden required to search the methods of using the animals or cells with the compounds, which have a different classification, would be undue.

With exception of arguments directly pertaining to Inventions II-V, which have been rejoined, the restriction requirement is still deemed proper and is therefore made **FINAL**.

Claims 1-34 are pending, however, claims 1-4, 13-16 and 31-33 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions, the requirement having been traversed in Paper No. 14. Claims 5-12 and 17-30 are under current examination.

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Priority

Acknowledgment is made of applicant's claim for domestic priority under 35 U.S.C. 119(e). The priority claimed by the applicant is, in part, denied. Support for claims 17-30, directed to a transgenic mouse with a disruption in the anaphylatoxin C3a receptor gene, wherein the transgenic mouse exhibits an abnormality in the thymus (claims 17-20,26-30), or increased susceptibility to seizure (claims 21,22 and 26-30), or exhibits a stimulus processing disorder (claims 23-30) was not found in provisional applications 60/215467 or 60/244083 filed 06/29/2000 and 10/26/2000, respectively. The priority documents fail to describe any of the claimed phenotypic characteristics claimed in the current application. Thus, only claims 5-12 are granted a priority date of 06/29/2000. Claims 17-30 are denied priority. ***Claim Rejections - 35***

USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-12,17-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 5-12,17-30 encompass more than one anaphylatoxin C3a receptor gene as they are drawn to "an anaphylatoxin C3a receptor gene" or "a anaphylatoxin C3a receptor gene". The claims encompass any anaphylatoxin C3a receptor gene that may exist in each and every species of animal. While the specification teaches that other anaphylatoxin genes exist, such as anaphylatoxin C5a (page 1, line 28), the specification teaches only one, mouse anaphylatoxin

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C3a receptor gene (SEQ ID NO:1) and does not disclose that other anaphylatoxin C3a receptor genes exist or have the same function as the anaphylatoxin C3a receptor gene disclosed. Therefore, adequate written description to support the claims encompassing more than the one, disclosed anaphylatoxin C3a receptor gene is lacking.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieve regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the anaphylatoxin C3a receptor gene encompassed by SEQ ID NO:1, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Claims 17 and 26 encompass a transgenic mouse with a disruption in the anaphylatoxin C3a receptor gene resulting in any abnormality of the thymus. However, the specification only reports a phenotype comprising reduced thymus weight, reduced thymus size or reduced

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thymus to body weight ratio in male homozygotes in comparison to a wild-type mouse thymus. Furthermore, the data presented in Table I (page 54) and Figure 3, demonstrate normal thymus size in female mice comprising a disruption in the anaphylatoxin C3a receptor gene (and a greater thymus/body weight in the case of the female mouse represented in Figure 3). Therefore, only a transgenic male mouse with a homozygous disruption in the anaphylatoxin C3a receptor gene and reduced weight, reduced size or reduced thymus to body weight ratio in comparison to a wild-type mouse thymus, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 5-12 and 17-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mouse or mouse cell whose genome comprises a homozygous disruption in the anaphylatoxin C3a receptor gene wherein said mouse is a male exhibiting reduced size and weight of the thymus, or said mouse is a male or female exhibiting increased susceptibility to seizure or a stimulus processing deficit, does not reasonably provide enablement for any transgenic non-human animal or a cell of any species with a disruption of any anaphylatoxin C3a receptor gene wherein said transgenic cell or animal has any phenotype. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 5-7, 9 and 27 are directed to a cell comprising a disruption in the anaphylatoxin C3a receptor gene. Claim 8 is directed to a non-human transgenic animal with a disruption in the anaphylatoxin C3a receptor gene. Claims 10 and 26 are directed to methods of producing a

transgenic mouse with a disruption in the anaphylatoxin C3a receptor gene. Claims 17-25, are directed to a transgenic mouse with a disruption in the anaphylatoxin C3a receptor gene, wherein the transgenic mouse exhibits an abnormality in the thymus (claims 17-20), or increased susceptibility to seizure (claims 21 and 22), or exhibits a stimulus processing disorder (claims 23-25). Claims 11, 12 and 28-30 are directed to methods of using a transgenic mouse with a disruption in the anaphylatoxin C3a receptor gene to screen for modulators of anaphylatoxin C3a receptor function or expression (claims 11,12) or modulator of a phenotype associated with the disruption of the anaphylatoxin C3a receptor gene (claims 28-30).

The state of the art at the time of filing was such that one of skill could not predict the phenotype of transgenics. Leonard (1995, Immunological Reviews, Vol. 148, pages 98-113) disclosed mice with a disruption in the g_c gene which were intended to be a model for X-linked severe combined immunodeficiency (XSCID), but display a variety of unexpected traits (abstract). These knockout mice were expected to have thymocytes with decreased proliferation in response to stimulation with antibodies, but the thymocytes proliferated normally (page 105, line 7). Moens (1993, Development, Vol. 119, pages 485-499) taught two mutations produced by homologous recombination in two different locations of the N-myc gene produce two different phenotypes in mouse embryonic stem cells, one leaky and one null (page 486, column 1, first full paragraph). Griffiths (1998, Microscopy Research and Technique, Vol. 41, pages 344-358) teaches that, despite a known role for the PLP gene based on spontaneous mutations in the gene, the knockout mouse failed to display any of the expected phenotypes (page 350, last paragraph). Thus, the phenotype of knockout mice was highly unpredictable.

The art at the time of filing further held that targeted gene insertion technology was not available for any species other than mouse. Since homologous recombination is required for gene targeting methods, embryonic stem cell technology must be available to carry out the

method. Mullins (1996, *J. Clin. Invest.*, Vol. 98, pages S37-S40) teach that non-mouse ES cells capable of providing germline chimeras were not available (page S38, column 1, first paragraph). Campbell and Wilmut (1997, *Theriogenology*, vol. 47, pp. 63-72) acknowledge reports of ES-like cells in a number of species, but emphasize that as yet there are no reports of any cells lines that contribute to the germ line in any species other than mouse (page 65). Furthermore, other potential methods of generating transgenic embryos using homologous recombination had not been developed at the time the invention was made (McGreath, 2000, *Nature*, Vol. 405, pages 1066-1069; Kent-First, 2000, *Nature Biotechnology*, Vol. 18, pages 928-929; Dinnyes, 2002, *Cloning and Stem Cells*, Vol. 4, pages 81-90). Thus, at the time of filing, knockout animals could not be prepared for any species other than mouse.

1) The specification does not provide adequate guidance for one of skill in the art to generate non-human transgenic animals having a disruption in the anaphylatoxin C3a receptor gene (claim 8) in any species other than mouse. The methods of gene targeting such as employed in the instant invention require embryonic stem cells. As stated above, the state of the art at the time of filing was that ES cell technology was not available for targeted mutagenesis in any species other than mouse. The specification discloses injecting cells comprising a disruption in the anaphylatoxin C3a receptor gene into a blastocyst to generate transgenic animals (page 15, lines 28-29). However, the specification and the art at the time of filing fail to disclose any ES cells other than mouse ES cells that contribute to the germline. Therefore, the guidance offered in the specification is limited to the production of knockout mice using mouse ES cells and no teachings or guidance are offered in regard to how one would have prepared any other species of animal using targeted mutagenesis. Without such guidance, it would require undue experimentation for one of skill in the art at the time of filing to make any

transgenic, non-human animal, other than mouse, with a disruption in the anaphylatoxin C3a receptor gene.

2) Applicants fail to enable making and/or using a transgenic anaphylatoxin C3a receptor knockout mouse having a phenotype other than a) reduced thymus size, thymus weight, or thymus/body weight ratio wherein the mouse is male, b) increased susceptibility to seizure or c) a stimulus processing deficit. The specification does not provide an enabled use for the knockout claimed that has a wild type phenotype or any other phenotype as encompassed by claim 8. The data provided in the specification does not support the claimed phenotype of reduced thymus size, thymus weight, or thymus/body weight ratio in female mutant mice as encompassed by claims 17-20 and 26. As set forth in the art, the phenotype of a transgenic, knockout animal was unpredictable at the time of filing. In support of this state of unpredictability, anaphylatoxin C3a receptor knockout mice generated by Kildsgaard (2000, Jour. Immunol., Vol. 165, pages 5406-5409), were reported to have a normal thymus (page 5401, column 2, paragraph 2) while the male anaphylatoxin C3a receptor knockout mice generated in the current invention were shown to have altered thymus size. The specification does not overcome the unpredictability inherent in generating knockout mice such that any phenotype in anaphylatoxin C3a receptor knockout mice could be obtained other those listed above as phenotypes a-c. Without such guidance, it would require one of skill in the art at the time the invention was made, undue experimentation to determine how to obtain any phenotype other than those listed above.

3) The specification fails to enable disrupting any anaphylatoxin C3a receptor gene in a mouse or any other species or a cell other than a mouse cell. The specification only teaches one anaphylatoxin C3a receptor gene (SEQ ID NO: 1). The specification does not provide adequate guidance for determining other anaphylatoxin C3a receptor genes or that other

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anaphylatoxin C3a receptor genes exist or have the same function as the anaphylatoxin C3a receptor gene disclosed. Limiting claims 5,8,10-12,17,21,23,26, and 28-30 to a transgenic mouse or mouse cell and deleting "a" or "an" preceding "anaphylatoxin C3a receptor" in claims 5,8,10-12,17,21,23,26, and 28-30, would overcome this rejection.

4) The specification does not enable making a mouse that is heterozygous for a disruption the anaphylatoxin C3a receptor gene with the phenotypes encompassed by claims 17-25. As set forth in the art, the phenotype of a transgenic, knockout animal was unpredictable at the time of filing. The specification does not teach how to make a mouse heterozygous for a disruption in the anaphylatoxin C3a receptor gene that displays any phenotypes other than wildtype. Thus, the specification does not overcome the unpredictability inherent in generating knockout mice such that any phenotype in heterozygous anaphylatoxin C3a receptor knockout mice could be obtained. Without such guidance, it would require one of skill in the art at the time the invention was made, undue experimentation to determine how to obtain make a mouse that is heterozygous for a disruption the anaphylatoxin C3a receptor gene with the phenotypes claimed in claims 17-25.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1) Claims 5-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Capecchi (*Scientific American*, 1994, vol. 270, pp 34-41) in view of Tornetta (1997, *J. Immunol.*, Vol. 158, pages 5277-5282).

Capecchi taught transforming a cell with a nucleic acid construct comprising a disruption in the HoxA-3 gene, resulting in an inactivating insertion of a selective marker gene into the endogenous HoxA-3 locus, and using said cell to generate a mouse whose genome comprises a disruption in the HoxA-3 gene. Capecchi differs from the claimed invention in that the targeting construct does not disrupt the anaphylatoxin C3a receptor gene.

However, at the time the claimed invention was made, Tornetta taught the cloning of the mouse anaphylatoxin C3a receptor gene (entire document and for further sequence detail GenBank Accession No. U77461).

Accordingly, it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made, to make cells and a knockout mouse having a disruption in a targeted gene as taught by Capecchi wherein the gene was the anaphylatoxin C3a receptor gene as taught by Tornetta. One of ordinary skill in the art would have been sufficiently motivated to replace the Hox3A gene with the anaphylatoxin C3a receptor gene, as it was an art-recognized goal to determine the physiological role of a gene of interest by the generation of a knockout mouse. One of ordinary skill in the art would have been sufficiently motivated to disrupt the anaphylatoxin C3a receptor gene to determine its role in inflammatory disease, as described by Tornetta (page 5277, column 2, lines 3-8). Tornetta further supports the motivation to generate a transgenic mouse comprising a disruption in the anaphylatoxin C3a receptor gene based on the success of a similar disruption in the anaphylatoxin C5a receptor gene substantiating a role of the anaphylatoxin C5a receptor gene in inflammatory disease (Tornetta, page 5277, column 1, last 2 lines-column 2 lines 1-3).

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Note that absent any phenotypic requirements for the claimed transgenic mouse, the combination of the cited prior art is sufficient to make obvious the claimed invention. Capecchi discloses the applicability of gene targeting to many other genes so that a correlation can be drawn between the malfunctioning gene and the manifestation of disease (page 41, column 2, 2nd full paragraph).

Thus, the claimed invention is clearly *prima facie* obvious in the absence of evidence to the contrary.

2) Claims 5-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beach (1999, USPN 5,919,997) in view of Tornetta (1997, J. Immunol., Vol. 158, pages 5277-5282).

Beach taught transforming a cell with a nucleic acid construct comprising a disruption in the INK4 gene, resulting in an inactivating insertion of a selective marker gene into the endogenous INK4 locus, and using said cell to generate a knockout mouse whose genome comprises a disruption in the INK4 gene (column 14, lines 61-66). Beach taught administering compounds to the transgenic knockout mice comprising a disruption in the INK4 gene to screen for agents that affect the INK4 mutant phenotype and modulate the expression or function of INK4 (column 26, lines 51-54 and claim 11). Beach differs from the claimed invention in that the targeting construct does not disrupt the anaphylatoxin C3a receptor gene.

However, at the time the claimed invention was made, Tornetta taught the cloning of the mouse anaphylatoxin C3a receptor gene (entire document and for further sequence detail GenBank Accession No. U77461).

Accordingly, it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made, to make cells and a knockout mouse having a disruption in a targeted gene as taught by Beach wherein the gene was anaphylatoxin C3a receptor as taught by Tornetta and to use said animals to screen for compounds that modulate anaphylatoxin C3a

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receptor expression or function by assessing changes in the anaphylatoxin C3a receptor mutant phenotype. One of ordinary skill in the art would have been sufficiently motivated to replace the INK4 gene with the anaphylatoxin C3a receptor gene, as it was an art-recognized goal to determine the physiological role of a gene of interest by the generation of a knockout mouse and to use the mouse to screen for agents that affects or ameliorates a mutant phenotype. One of ordinary skill in the art would have been sufficiently motivated to disrupt the anaphylatoxin C3a receptor gene to screen for modulators of anaphylatoxin C3a receptor expression or function as a means of identifying drugs that treat the phenotypes associated with loss of anaphylatoxin C3a function.

Thus, the claimed invention is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is 703-305-5469. The examiner can normally be reached on 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on 703-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Valarie Bertoglio
Patent Examiner


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